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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/807,783	06/01/2001	Jingye Liu	CCP-100	4651

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EXAMINER	
FOLEY, SHANON A	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 05/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/807,783	LIU ET AL.	
	Examiner	Art Unit	
	Shanon Foley	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 February 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5-8,11,12,16 and 18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5-8,11,12,16 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

In the response received February 9, 2004, applicant amended claims 1 and 6. Claims 1, 3, 5-8, 11, 12, 16 and 18 are pending and under consideration. Applicant's arguments, have been fully considered and are persuasive. Therefore, the rejection under 35 U.S.C. § 103 has been withdrawn. However, upon further consideration of the prior art, a new ground(s) of rejection are made. In addition, previous indication of allowable subject matter is withdrawn. The examiner regrets any inconvenience applicant experiences.

Specification

The substitute specification filed October 5, 2001 is compliant with 37 CFR § 1.125 and has been entered. However, in paragraphs 5 and 6 of the new specification, there is a discrepancy between "92114998" in paragraph 5 and "92114988" in paragraph 6. In either case, the examiner is unable to find any of the patents "CN Patent Nos. 85107525", "92114998" and "92114988" cited in the specification. It is not clear whether the patent numbers contain typos or if they are just not publicly available from any patent database. Applicant is required to correct any typos that may be present in the patent numbers. It would also be appreciated if applicant provided copies of these documents to the Office. The disclosure is also objected to because of the following informalities: In lines 2-3 of paragraph 7, the specification recites "satisfactory unsatisfactory". "Satisfactory" should be deleted. In addition, line 3 of paragraph 20 and line 4 of paragraph 21 recite, "Pavamyxovirus", instead of "Paramyxovirus".

Appropriate correction is required.

Claim Objections

Claim 16 is objected to because of the following informalities: "wherein said stabilizer comprises" is repeated in line 2. Appropriate correction is required.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3, 5-8, 12 and 16 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3, 4, 6, 7, 9-13, 15 and 16 of U.S. Patent No. 6,562,350 B1 (Wang et al.) in view of U.S. Patent No. 6,013,264 (Petre et al.).

Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant formulation "comprises" a live, attenuated, lyophilized hepatitis A vaccine and does not exclude other vaccine antigens. One of ordinary skill in the art at the time the invention was made would have been motivated form a heat-stable multivalent vaccine to avoid multiple injections and prevent multiple diseases, see column 1, lines 21-25, column 2, line 66 to column 3, line 2 and claims 1, 6, 9 and 11 of Petre et al.

The instant claims also recite specific ranges of grams per liter of the various stabilizer ingredients. However, the amounts recited are equivalent to the percent ranges recited by Wang et al. (6,562,350 B1).

Therefore, the instant invention is not patentably distinct from US 6,562,350 B1.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 18 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 18 recites the limitation "said lyophilizing step" in line 1. There is insufficient antecedent basis for this limitation in the claim. It is noted that if claim 18 were to properly depend from claim 6, which is the only claim that recites a lyophilizing step, claim 18 would be a duplicate of claim 11. Therefore, it is suggested that applicant cancel claim 18.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 5, 6, 11, 16 and 18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the live, attenuated hepatitis A from the wild-type HAV strain L-A-I is required to practice the claimed invention because it is a necessary limitation for the success of the invention as stated in claim 1. The reference strain L-A-I is also required to practice the invention since the instant vaccine strain is required to be prepared from it. As a required element it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the enablement requirements of 35 U.S.C. § 112, first paragraph, may be satisfied by a deposit of the attenuated strain claimed. See 37 CFR § 1.802. One cannot practice the claimed invention without the live, attenuated hepatitis A strain or the L-A-I strain from which it is derived. Further, one cannot determine whether an HAV has the necessary characteristics without access to the parent L-A-I or the live, attenuated hepatitis A claimed. Therefore, access to the live, attenuated hepatitis A from the wild-type HAV strain L-A-I and the parent strain L-A-I are required to practice the invention. On page 2, paragraph 6 of the specification, reference is made to vaccine strains prepared from L-A-I. However, there is no indication whether this strain is publicly available. There is no disclosure provided for how the vaccine strain is "prepared from" the reference strain, L-A-I, or what characteristics are required. The disclosure does not provide a repeatable method for readily identifying a live, attenuated hepatitis A from the wild-type HAV strain L-A-I and it does not appear to be readily available material.

Deposit of the live, attenuated hepatitis A from the wild-type HAV strain L-A-I and the parent strain, L-A-I, in a recognized deposit facility would satisfy the enablement requirements

of 35 U.S.C. 112., because the strains would be readily available to the public to practice the invention claimed, see 37 CFR § 1.801- 37 CFR § 1.809.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR § 1.808.

If a deposit is not made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and that the following criteria have been met:

(a) during the pendency of this application, access to the invention will be afforded to one determined by the Commissioner to be entitled thereto;

(b) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;

(d) a viability statement in accordance with the provisions of 37 CFR 1.807; and

(e) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

In addition the identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.803 - 37 CFR 1.809 for additional explanation of these requirements.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 1 rejected under 35 U.S.C. 103(a) as being unpatentable over and McAleer et al. (US 4,147,772) and Lemon et al. (US 5,766,906).

Claim 1 is drawn to a stabilized, lyophilized hepatitis A vaccine formulation comprising prophylactically effective titers of a live, attenuated hepatitis A virus prepared from the wild-type HAV strain L-A-I and a stabilizer at a concentration sufficient to stabilize the virus against heat inactivation.

McAleer et al. teach a vaccine comprising an attenuated virus in a stabilizer that is lyophilized. The attenuated virus is a hepatitis virus, see claims 1, 4, 7, 8 and 10. McAleer et al. do not specifically recite hepatitis A.

However, Lemon et al. teach a live, attenuated hepatitis A vaccine in a vaccine formulation, see claims 7-10. Since the attenuating characteristics of the live, attenuated HAV prepared from the wild-type HAV strain L-A-I instantly claimed cannot be determined, the live,

attenuated HAV vaccine of Lemon et al. is viewed as equivalent. In any case, it is maintained that the skilled artisan would have been motivated to incorporate a known, efficacious HAV vaccine into the stabilized, lyophilized composition of McAleer et al. to increase storage stability and obtain an HAV vaccine that is quickly soluble when ready to use, see column 1, lines 56-58 of McAleer et al. Further, one of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of lyophilizing a known live, attenuated HAV vaccine, e.g. the vaccine of Lemon et al., with the composition of McAleer et al. because the stabilized, lyophilized formulation of McAleer et al. encompasses any hepatitis vaccine and the attenuated HAV vaccine of Lemon et al. also contains a stabilizer, see column 5, lines 56-61, and is administered by respiration of a solid particles in an aerosol form, see column 6, lines 28-40. Therefore, the invention would have been prima facie obvious to one of ordinary skill in the art, absent unexpected results to the contrary.

Applicant states on page 5 of the response that there is no reasonable expectation of success in the prior art for producing a live, lyophilized picornavius vaccine strain. However, the teachings of McAleer et al. teach live, attenuated picornavirus vaccines, i.e. polio and hepatitis, that have been lyophilized, see the previous citations. This reference, in combination with the HAV vaccine of Lemon et al. renders the invention prima facie obvious. The burden is on applicant to provide evidence that the combination of McAleer et al. and Lemon et al. would not have resulted in a reasonable expectation of success. *In re Sasse*, 629 F.2d 675. 207 USPQ 107 (CCPA) 1980. See also MPEP § 716.07.

Claims 3, 5-8, 11, 12, 16 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over McAleer et al. and Lemon et al. *supra*, as applied to claim 1 above, and further

in view of McAleer et al. (US 4,338,335), Volkin et al. (US 6,051,238) and Francon et al. (US 5,075,110) and Pratt et al. (US 3,557,524).

The claims are drawn to a stabilized vaccine formulation comprising a live, attenuated HAV vaccine or a stabilizer comprising human serum albumin and/or gelatin, trehalose, at least one amino acid or an alkali metal salt of glutamic acid, aspartic acid, arginine, or lysine, ascorbic acid, urea, mannitol and/or sorbitol, and inositol. The claims also encompass a method of preparing a stabilized vaccine. The claims also recite concentrations of each ingredient in the stabilizing composition and steps for lyophilization.

McAleer et al. (US 4,147,772) teach a method of stabilizing a vaccine by combining a vaccine with a stabilizer, see claim 10. The stabilizer of McAleer et al. comprises gelatin, sorbitol and mannitol, see claim 1. McAleer et al. do not teach or suggest trehalose or ascorbic acid.

However, Volkin et al. teach live, attenuated hepatitis vaccine formulations that are lyophilized comprising gelatin, human serum albumin, sorbitol, ascorbic acid and trehalose, see column 6, line 13 to column 9, line 4.

Neither McAleer et al. (US 4,147,772) nor Volkin et al. teach or suggest at least one amino acid or an alkali metal salt of glutamic acid, aspartic acid, arginine, or lysine.

McAleer et al. (US 4,338,335) teach that glutamic acid and arginine are vaccine stabilizers for vaccines comprising enteroviruses, i.e. hepatitis and polio, see column 2, lines 32-40.

McAleer et al. (US 4,147,772), McAleer et al. (US 4,338,335) nor Volkin et al. teach urea.

However, Francon et al. (US 5,075,110) teach urea as a stabilizing component for attenuated, lyophilized vaccines comprising urea, see claims 1 and 2.

McAleer et al. (US 4,147,772), McAleer et al. (US 4,338,335), Volkin et al. nor Francon et al. suggest inositol.

However, Pratt et al. (US 3,557,524) teach inositol as a stabilizing agent for attenuated vaccines, see column 3, lines 10-33.

MPEP § 2144.06 recites the conclusions of *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA), "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose...[T]he idea of combining them flows logically from their having been individually taught in the prior art." The instant invention combines old ingredients of known stabilizers. Since each of the ingredients in the instant stabilizing composition are known in the prior art as conventional vaccine stabilizing components, the combination of their additive effects renders the invention prima facie obvious and does not exhibit an unexpected result.

Although none of the references teach the ratio of virus to stabilizer or the range of ingredients recited, or the specific lyophilizing steps, differences in concentration and temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (571) 272-0898. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Shanon Foley

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